Specification

METHOD FOR TISSUE TREATMENT WITH INJECTED SUBSTANCE

Background of the Invention

Related Cases

This application is a Continuation-in-Part of copending U.S. Patent Application Serial No. 09/510,537 filed February 22, 2000 which is a Continuation-in-Part of copending U.S. Patent Application Serial No. 09/105,896 filed June 26, 1998.

Field of the Invention

The present invention relates generally to methods and apparatus for body tissue treatment using injection apparatus, and more particularly to a method wherein a treatment substance is injected in the form of a highly viscous material for retarding substance disbursement to cause selective tissue necrosis in a controlled area of treatment, and to enhance and localize the use of substances for tissue necrosis by injecting a conductive viscous material to act as an electrode extension with simultaneous application of radio frequency (RF) energy.

Description of the Prior Art

Various methods of treating diseased body tissue have been employed, including surgical removal, freezing and treatment with chemical agents and RF energy. A variety of treatment fluids are currently known to be of benefit in treating diseased tissue. For example, there are a number of tumor suppressor genes, viral vectors, markers, vaccines, enzymes, proteins and biological agents that can be used for gene therapy and cancer treatment. The current method of delivery of these substances is to inject them into the blood stream through use of a conventional needle and syringe. The result is that the substance is carried by the blood to every part of the body. In many cases, it would be advantageous to be able to treat only a particular organ, or part of an organ.

Attempts to destroy diseased tissue with RF energy are limited in success due in part to a lack of technology to cause larger tissue lesions using RF energy through small incisions in the body. A common technique of RF energy application known as "monopolar" mode applies RF

energy to large areas of healthy tissue as well as the diseased portion. In this case, a single RF input electrode is positioned near the diseased tissue, and a return electrode, usually in the form of a plate is positioned on the outside of the body. Application of RF energy in what is known as "bipolar" mode restricts the energy distribution, but requires precision placement of at least two electrodes.

The treatment of diseased tissue is aided by use of laparoscopic/endoscopic surgical instruments that allow a surgeon to see inside the body cavity of a patient without the necessity of large incisions. This reduces the chances of infection and other complications related to large incisions. The endoscope further allows the surgeon to manipulate microsurgical instruments without impeding the surgeon's view of the area under consideration. Although endoscopic surgical instruments are well developed and in use for surgical operations, an apparatus and method is not described or used in the prior art for delivering a treatment fluid interstitially to a precise target area within a body.

It is therefore apparent that there is a need for an improved method of treating diseased tissue, including an apparatus that can deliver a treatment fluid to an interior localized body area. There is also a need for a method providing greater control over the volume of tissue treated in the use of RF energy therapy.

SUMMARY OF THE INVENTION

It is therefore an object of the present invention to provide an improved method of treating a localized volume of body tissue.

It is a further object of the present invention to provide a method of localized tissue treatment by injecting a treatment substance in the form of a gel.

It is another object of the present invention to provide a method of tissue therapy including the injection of an electrically conductive substance for concentrating applied RF energy by effectively extending the range of an RF electrode.

It is a still further object of the present invention to provide a method of body tissue therapy wherein a needle is inserted through a biopsy needle guide for application of a

conductive treatment substance, and wherein RF energy is applied through an electrically conductive needle.

It is another object of the present invention to provide a method of injecting a specific treatment substance to a localized interior body part.

It is an object of the present invention to provide a method of applying a treatment substance to a localized body portion by guiding a needle with an endoscopic surgical instrument.

It is a further object of the present invention to provide a method of injecting a treatment substance to a localized body portion by guiding a needle through the body to the localized portion by use of a non-invasive imaging device.

Briefly, a preferred embodiment of the present invention includes a method wherein a viscous treatment substance is injected into a diseased portion of body tissue for the purpose of localized, selective necrosis of target tissue by resisting substance migration. The treatment substance injected is in the form of a gel, or alternatively in the form of microspheres. Localized treatment is further enhanced by including a conductive component in the treatment substance, and while injecting the substance, simultaneously applying RF (radio frequency) energy to an injection needle acting as an RF electrode. The conductive gel serves as an extension of the electrode, thereby localizing and enhancing treatment in the volume penetrated by the gel. Improved positioning of the injection needle is aided with the use of ultrasound imaging with clarity enhanced by inclusion of imaging enhancement agents in the gel. Alternatively, microspheres are filled with a gel/solution and gas combination providing contrasting areas of ultrasound reflection.

An advantage of the present invention is that it allows a lethal fluid to be injected into a tumor without seriously affecting the surrounding healthy tissue.

A further advantage of the present invention is that it provides a selective treatment of cancer cells, avoiding the need to inject toxic substances throughout a patient's body.

A still further advantage of the present invention is that it provides enhanced control of a volume of tissue being treated with substances and radio frequency energy.

Brief Description of the Drawings

Fig. 1a illustrates various organs that can be treated according to the present invention;

Fig. 1b shows transperineal injection for treating the prostate;

Fig. 2 shows a microsphere;

Fig. 3 illustrates various alternate methods of treatment of an organ, showing treatment of a prostate;

Fig. 4 illustrates transurethral treatment of a prostate;

Fig. 5 illustrates a biopsy apparatus as used in the present invention, and as applied to treatment of a breast;

Fig. 6 illustrates various components of a gel;

Fig. 7 is a list of therapy substances;

Fig. 8 is a list of electrically conductive material for use in a gel, or in a microsphere;

Fig. 9 is a list of binding/gelling agents;

Fig. 10 lists image contrast agents;

Fig. 11 illustrates components of a microsphere; and

Fig. 12 is a flow chart of the method of the present invention.

Detailed Description of the Preferred Embodiments

A preferred embodiment of the method of the present invention will now be described in reference to Figs. 1a, 1b and 2 of the drawing. According to the present invention, a tissue treatment substance is prepared and includes a chemical agent and a binding agent formulated to

migrate slowly upon injection into tissue. The objective is to allow the chemical agent a lengthened amount of time in contact with the desired treatment area. The substance is injected into the diseased body portion through use of any one of various devices known to those skilled in the art. This is illustrated in Fig. 1a figuratively illustrating injection devices 10, which can be applied to any organ as required. For example, devices that can be used for substance injection are described for use in fluid injection in U.S. Patent Serial Numbers 09/510,537 and 09/105,896. The entire contents of these applications are incorporated in the present disclosure by reference. Another type of device known as a biopsy device can also be used, and is described in the following specification in reference to Fig. 5. A laparoscope device, known to those skilled in the art, can be inserted through an incision for use in guiding an injection needle to a target tissue in the liver 12, kidney 14, uterus 16, bladder 18, and lung 20, of Fig. 1a, as well as other organs not shown. A convenient device for injection into a breast 22 is the apparatus of a biopsy device, with the usual biopsy probe replaced with a hollow core needle. This will be described in reference to Fig. 5. Fig. 1b shows the prostate 24, with a transperineal insertion of a needle. The biopsy device is a convenient tool for this procedure. In guiding a needle to a precise target, the optics of a laparascope or other similar device is often helpful. The use of a non-invasive ultrasound imaging technique is also included in the spirit of the invention for guiding a needle. This is helpful in guiding a biopsy device, and can also be used as an additional optional aid when using a laparascope or similar device. The use of an ultrasound probe and a biopsy device inserted into the rectum for inserting a needle through the rectum wall for injection into the prostate will be described in detail in the following text and drawing.

Preferred forms of the viscous substance include a gel and microspheres. Fig. 2 illustrates the construction of a microsphere 26 with a treatment material 28 captured inside. The microsphere 26 is constructed of a biodegradable material. The gradual deterioration of a plurality of microspheres upon injection provides a slow time release of the treatment material 28.

Fig. 3 illustrates various alternate embodiments of the present invention. A particularly important embodiment includes the application of RF (radio frequency) energy to a target simultaneously with injection of a substance having an electrically conductive property. Fig. 3

shows a biopsy device 30 with an RF input connector 32 for connection of an active side 34 of an RF power supply 36. The device 30 includes construction (not shown) that connects the RF input line 38 electrically to an electrically conductive injection needle 40. The return side 46 of the power supply can also be connected to a connector 32 for making electrical contact with a conductive outer sleeve 42. This is indicated by line 44. Alternatively, device 30 can include one or more additional electrodes 48, insulated from needle 40, and can provide connection of these electrodes with the line 44 to provide localized RF. This approach is known as a bipolar mode of operation. Alternatively, the passive/return side 46 can be connected by a line 50 to a conductive plate 52 positioned at the outside of the body 54. This approach is known as a monopolar mode of operation. According to the present invention the conductive substance is injected while simultaneously applying RF energy. The result is that the conductive substance serves as an effective electrode extension, and the area of RF energy is concentrated in the volume of tissue 56 infused by the conductive substance. The biopsy device 30 is equipped in this application with a substance injection syringe 58, replacing the conventional biopsy probe. Fig. 3 clearly illustrates a transrectal approach to treating the prostate using an ultrasound imaging device 60, inserted into the rectum 62 for guiding the biopsy probe 42 into the rectum 62 and for guiding the needle 40 into the prostate 64.

The use of a conductive treatment substance in combination with RF energy as illustrated by example in Fig. 3 also applies to any other organ in need of such treatment, particularly including those referred to in reference to Fig. 1a. The construction and use of the various endoscopes, laparoscopes, etc. with RF energy in bipolar or monopolar mode will be understood by those skilled in the art after reading the present disclosure and the incorporated reference applications, including U.S. Patent Application Serial Numbers 09/105,896 and 09/510,537.

Transperineal injection, wherein a needle is inserted percutaneously between the rectum and pubic area into the prostate as shown in Fig. 1b, is further described in detail in Serial Number 09/510,537 in reference to Fig. 17 therein. Transrectal injection of the prostate was discussed above in reference to Fig. 3. Referring now to Fig. 4, a transurethral approach to the prostate is described. An injector apparatus 68 with the aid of a non-invasive imaging device 70, and/or an ultrasonic probe in the rectum as referred to above, is used to inject treatment fluid

into the prostate 66. The apparatus 68 includes an adjustable portion 72 with a scale 74 for extending and retracting a flexible hollow core needle 76, and a syringe apparatus 78 for injection of a substance through the needle 7c. The apparatus 68 is constructed in a similar manner to the apparatus of Fig. 3 in Serial No. 09/510,537 and Fig. 25 in Serial No. 09/105,896. The probe 80 in apparatus 68 differs from the probe 24 of Fig. 3 in Serial No. 09/510,537. Probe 80 is flexible, allowing some conformance to a urethra 82, or other opening as required. The needle 76 is shown bent upward with the tip 84 positioned in the prostate 66. In order to accomplish the bend in the needle, the needle can either be pre-stressed to direct it at an angle upon leaving the probe 80 as described in detail in Serial No. 09/105,896, or a bellows and wire apparatus can be used as described in Serial No. 09/105,896. To incorporate the bellows and wire, an extra sheath employing the bellows and wire can be provided inside the catheter through which the needle extends. Alternatively, the sheath can serve as the catheter. As a further alternative, a larger probe such as probe 24 in Fig. 3 of Serial No. 09/510,537 can be used to incorporate the apparatus described in reference to Figs. 24 and 25 of Serial No. 09/105,896, including the guide wire 293 and sheath 290. The wire tensioning apparatus is described symbolically as item 86 in Fig. 4 of the present disclosure.

An alternate embodiment of the method and apparatus for treating the prostate includes the use of a cystoscope (endoscope), such as endoscope 22 of Fig. 1 in Serial No. 09/510,537, to place the needle near the prostate, and then to use the pretensioned needle or wire and sheath apparatus to direct the needle at an angle. The needle is then extended using the apparatus, with the depth of penetration through the urethra wall and into the prostate monitored through use of a scale, or through use of non-invasive imaging equipment, and/or an ultrasound probe, all as described in U.S. Patent Application Serial No. 09/510,537.

Fig. 4 of the present application also shows a bladder 88 and rectum 90, as examples of organs that can be reached and treated through use of the method of the present invention.

As a further embodiment, a flexible ultrasonic probe can be included inside a catheter, such as catheter 80, or inside the needle 76 of the device shown in Fig. 4. The flexible ultrasonic probe can be inserted inside the needle 76 through an access line as indicated in Fig. 4 by dashed

lines 92 from an ultrasound transceiver 94, entering injector 78 from the side. In the case where the probe is carried alongside the needle 76 in the catheter 80, the flexible probe can be inserted separately, as indicated by lines 96.

Fig. 5 shows further detail of a biopsy device 96, and demonstrates its use in treating a breast 98. the device 96 can also be used according to the present invention to treat the other body organs. A first probe device 100 includes a cannula 102 for puncturing through the skin/tissue as shown. In doing a biopsy, a probe apparatus 104 is inserted through the cannula 102. The biopsy probe 104 has a sharp hook 106 at a distal end for engaging, capturing and retrieving body tissue. According to the present invention, the probe 104 is left out and a hollow core needle 108 is inserted through the cannula 102. The needle 108 is connected to a syringe 110 by way of a Leur hub 112 to a housing 114. The needle 108 can further penetrate the tissue to a required depth 116, and a treatment substance is injected to a volume of tissue 118. For application of RF energy as discussed above, the needle 108 is connected to an RF input connector 120 through housing 114. For monopolar operation, a plate 122 can be placed outside the breast 98 with an RF return line 124 attached and connected to the RF power supply. For bipolar operation, various configurations are possible, as discussed above. For example, the needle 18 can have insulation 126 for electrically separating the conductive needle 108 from the conductive cannula 102. The cannula 102 is electrically attached to a connector 128 for attachment to an electrical return line to the RF power supply. Various alternative arrangements will be apparent to those skilled in the art and are included in the present invention.

Fig. 6 shows the components in a gel for use in the present invention. A gel 130 includes a treatment substance 132 and a binding/gelling agent 134. In addition, a gel can include an electrically conductive element 136, and/or a contrast agent 138.

A list of various treatment substances is given in Fig. 7. A gel or liquid can contain any combination of these or other treatment substances as required and can be used directly as a gel or liquid, or can be enclosed in microspheres. Some of the representative substances can have dual purposes. For example, saline solution and acetic acid are electrically conductive and are therefore also included under the list of conductive substances in Fig. 8. A list of binding/

gelling agents is shown in Fig. 9, and contrast agents are listed in Fig. 10. A contrast agent is a substance that enhances an image. Numerous agents for enhancing an ultrasound image, for example, are well known to those skilled in the art of imaging, and include dyes and various other substances such as barium sulfate, etc. Including a contrast agent in the gel or microspheres enhances the image.

The construction of a microsphere 140 as a substance for use in the present invention is more clearly illustrated in reference to Fig. 11. A sealed container 142 is shown in cross section, and can have any shape i.e. oval, cylindrical, etc., and with its contents will be referred to generally as a microsphere. The purpose of the microsphere 140 is to carry a substance 144 to a target tissue, and through gradual absorption/disintegration of the container 142, will provide a corresponding gradual release of the treatment substance 144. The microsphere 140 also does not migrate/diffuse as rapidly as a liquid, and therefore allows more control of the area/volume of tissue being treated. The substance 144 can be a gel 146 with elements selected as discussed in reference to Figs. 6-9, or it can be a liquid 148 with similar components including a treatment substance 150 and as required/desired a conductive material 152 and/or a contrast agent 154. The microsphere 140 also preferably contains a gas 156 which can be any of various gasses, such as air, helium, fluorocarbons, etc. as noted in block 158. The microsphere container 142 and contents 144 and 156 are formed by combining a biomaterial or biodegradable polymer 160 (for forming the wall 142) with the substance 144 along with the gas 156 in a pressurized form. The details of such a process are well known to those skilled in the art and need not be described in detail herein.

The microsphere 140 structure also provides echogenic enhancement/image enhancement during ultrasound imaging. The gas 156 and substance 144 do not mix well, and the two materials (gas vs. gel/liquid) reflect sound differently, which creates a recognizable reflection/image of the substance and therefore area of treatment. As noted above, the substance 144 can also include an image enhancement component.

The preferred method of the present invention will now be described in reference to the flow chart of Fig. 12. A hollow core needle, or probe and hollow core needle or catheter is/are

inserted into a patient's body (block 162) through an appropriate opening, such as an incision, or through a natural passageway such as a urethra or cervical canal, rectum, etc. If a catheter or probe is used, the hollow core needle can be inserted through the probe or catheter either before or after insertion of the probe or catheter in the body. Through use of an endoscope, and/or a non-invasive detection positioning and imaging method, for example using ultrasound, etc., the user accurately positions the needle near a site to be treated (block 164). Having arrived near the target area, either an endoscope and/or non-invasive detection and imaging methods such as X-RAY, CT SCAN, MRI, ultrasound, fluoroscopy, etc. can be used to guide the needle or an appropriate needle assembly to a target area to be treated, and to monitor injection of the treatment substance. The needle assembly can be solely for application or injection of a substance to a precise target tissue location, or it can be additionally for application of RF energy.

In the case when RF energy is to be applied to the needle(s), the needle(s) are electrically conductive. The RF application can be monopolar wherein the energy is applied to one or more needles and an electrical return path is provided through a conductor placed exterior of the body, such as a conductive plate with a conductor line attached to the energy power supply return. Alternatively, the energy can be applied in a bipolar mode, wherein an electrical return path is provided locally, inside the body and near the needle/probe, etc. used to carry the RF energy into the body. The substance can be of a single type or a combination of substances, and as described above, and can be in the form of a gel, semi-liquid, a suspension, foam, viscous biomaterial or microsphere. The substance can include an electrically conductive component, or the substance can be non-conductive. In the embodiment wherein RF energy is transmitted along the needle while injecting an RF conductive substance, the substance serves as an effective extension of the needle/electrode providing enhanced RF energy application to the volume of tissue penetrated by the substance.

According to the method of the present invention, the needle is used either to apply a substance to a tissue surface, or is advanced interstitially into body tissue in need of treatment (block 164), the needle depth being observed by use of any of various methods, such as those listed including an endoscope for viewing marks on the needle, etc., a scale on the injector or

probe handle, or noninvasive imaging and position detection using X-RAY, CT scan, fluoroscopy, ultrasound etc.

For the purpose of the present disclosure, a non-invasive imaging technique is defined as any technique that allows observation of tissue or structure such as a needle in tissue without the use of additional invasive equipment for providing a view using visual light, such as the use of an endoscope or actual cutting away of tissue for a direct view. An ultrasound probe, for example, could be inserted by any means, through a natural opening, or through an incision to a point of interest, and then could provide a non-invasive view of an area beyond the probe through use of ultrasound imaging equipment. This use is termed non-invasive in the present disclosure.

The preferred embodiment of the invention includes an apparatus and method for directing a needle to a target area by bending the needle. This is particularly useful in the application wherein a flexible needle assembly is passed inside a catheter through a urethra to the vicinity of a prostate. A needle guiding apparatus is then used to deflect the needle tip toward the specific target area in the prostate.

With the needle tip at the target tissue, the treatment substance is injected (block 166) into the specific target tissue without affecting the surrounding area. The method can also, as an alternative/optional embodiment, include the application of RF energy upon injection of the substance. The substance can be either conductive or non-conductive. In the embodiment wherein the substance is conductive, the RF energy travels along the needle to the needle tip, and then continues to pass through the conductive substance acting as an extension of the needle/electrode and enhancing the RF energy in the volume of tissue treated by the substance. The application of RF energy can be for either causing hyperthemia or for causing tissue necrosis. Upon completion of treatment of the selected volume, the needle is removed from the treatment site (block 168).

At this point the apparatus can be either removed, or a new site in need of treatment can be identified and therapy applied. The process of identification is indicated by block 170. In the case where an endoscope is used, with or without the aid of observation with X-RAY, CT scan,

fluoroscopy or ultrasound, the probe can be moved to observe additional tissue to determine further areas in need of treatment. If observation is limited to X-RAY, CT scan, fluoroscopy, ultrasound, these tools are used alone to determine any additional targeted treatment areas. In either of the tool combinations noted above, they are used to precisely locate the targeted treatment area, place and/or insert the needle to the desired depth, and observe the substance flow and effect on the tissue. If no further treatment is required, the probe, needle assembly, and endoscope (if present) are removed (block 172). If further treatment is required, the probe and needle are positioned accordingly (block 164) and the needle is used to apply the substance to the tissue surface, or it is advanced into the tissue, and a sufficient volume of the substance is injected (block 166).

In applications for destruction/death of tissue, the necrossing agent can be combined with carrier agents and/or an anesthetic agent and/or with an antibiotic. Anesthetic agents, for example, include Lidocaine, Markaine and Sensorcaine as listed in Fig. 7, and other anesthetic agents known by those skilled in the art. Similarly, antibiotic agents include the various products known in the art.

The method of the present invention also has a significant advantage in gene therapy. In this case the application of RF energy for causing tissue death is generally not applicable. However, a smaller amount of RF energy can be applied for the purpose of raising the tissue temperature, i.e. creating hyperthermia to enhance a process. The prior art method of gene delivery injects genes into the body intravenously or intra-arterially using a conventional needle. This distributes the genes throughout the body. Ideally, the genes should be confined to the target area. Genes are listed in Fig. 7, as are other substances that for many illnesses, such as the treatment of tumors, should optimally be injected directly into the tumor or other target tissue. These include viruses, vaccines, proteins, tumor suppression genes, inhibitors, markers, and other biological agents. The substances that can be used in accordance with the therapy of the present invention also include mixtures of the above listed items and other chemicals, agents and their solutions in the form of gel, or suspensions, liquids or semi-liquids in microspheres that will be understood by those skilled in the art.

The method of Fig. 12 according to the present invention is meant to cover treatment of any body part. A most important embodiment is the method of the present invention applied to causing selective tissue necrosis, with or without the application of RF energy. Preferred embodiments of the present invention include treatment of the prostate, kidney, uterine myoma, fibroids, liver, ovarian cancer, bladder cancer, breast tumors and cysts (benign or malignant), and stomach, lung, colon and brain cancer, etc., and in the procedure of endometrial ablation of the uterine lining. An important embodiment in use with male patients is treatment of BPH (benign Prostatic Hyperplenia), enlarged prostate growth and prostate cancer. In this case, the needle can be inserted transurethrally, transrectally, or transperineally with or without an incision. The probe can also be inserted transperineally or transrectally (through the rectum) with or without incision under imaging guidance.

The method of the present invention is not limited to using the endoscope apparatus discussed herein and in Serial Nos. 09/105,896 and 09/510,537. Any type of scope apparatus that can be used to guide a needle to a target area is applicable to the method, such as cystoscopes, endoscopes, hysteroscopes, laparoscopes, bronchoscopes, gasteroscopes, etc. As mentioned above, a biopsy apparatus can also be used.

Although the present invention has been described above in terms of a specific embodiment, it is anticipated that alterations and modifications thereof will no doubt become apparent to those skilled in the art. It is therefore intended that the following claims be interpreted as covering all such alterations and modifications as fall within the true spirit and scope of the invention.

WHAT IS CLAIMED IS: